P1715R1

WE CLAIM:

- 1. A method of inducing hair cell generation or inner-ear-supporting cell growth, regeneration, and/or proliferation, comprising contacting an inner-ear-supporting cell which expresses HER2 and/or HER3 receptors with an effective amount of an isolated ligand which activates HER2 and/or HER3 receptors or a combination thereof.
- 2. The method of Claim 1, wherein the activating ligand is a heregulin polypeptide, heregulin variant, heregulin agonist antibody or fragment thereof capable of binding to the HER2 or HER3 receptor.
 - 3. The method of Claim 2, wherein the activating ligand is human heregulin or a fragment thereof.
- 4. The method of Claim 2, wherein the activating ligand is selected from the group consisting of HRG- α , - β 1, - β 2, (β 2-like) and - β 3 and fragments thereof.
 - The method of Claim 2, wherein the activating ligand is γ-HRG or a fragment thereof.
- 6. The method of Claim 2, wherein the activating ligand is recombinant human heregulin or a fragment thereof.
 - The method of claim 2, wherein the supporting sell is in cochlear implant.
- 8. The method of Claim 1, wherein the activating ligand is administered at a daily dose of about 1 μ g/kg to100 mg/kg.
 - 9. The method of Claim 2, wherein the activating ligand is an agonist antibody.
- 10. The method of Claim 1, wherein the contacting is by administration to a patient in need thereof.
 - 11. The method of Claim 6, wherein the heregulin is rHRG-β1-177-244.
 - 12. The method of Claim 1, wherein the inner-ear-supporting cell is in the utricle or cochlea.
- 13. The method of Claim 1 wherein the inner-ear-supporting cell expresses HER2, HER3, or both.
- A method of increasing the number of inner ear supporting cells, comprising administering to a patient in need thereof an effective amount of an isolated HER2 and/or HER3 activating ligand.
- 15. The method of Claim 14, wherein the activating ligand is a heregulin polypeptide, heregulin variant, heregulin agenist antibody or fragment thereof capable of binding to the HER2 and/or HER3 receptor.
- 16. A method of treating a pair cell related hearing disorder, comprising administering to a patient in need thereof an effective amount of an isolated HER2 and/or HER3 activating ligand.
- 17. The method of Claim 16, wherein the activating ligand is a heregulin polypeptide, heregulin variant, heregulin agonist antibody or fragment thereof capable of binding to the HER2 and/or HER3 receptor.
 - 18. A method, comprising the steps of:
 - (a) obtaining an inner-ear-supporting cell sample from a mammal;
- (b) contacting the sample with a ligand which activates HER2 or HER3 or a combination thereof to induce growth and/or proliferation of inner-ear-supporting cells in the sample and to obtain an expanded sample; and
 - (c) re-introducing the expanded sample into the mammal.

5 P3 10

II)

15

20

25

35

40

Sub 30

odd >